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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,232	12/12/2003	Yosser Ben Achour	02356.0087	4579

22852 7590 11/07/2005

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 11/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/733,232	BEN ACHOUR ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1,4-15 and 23-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3 and 16-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-35* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II in the reply filed on August 15, 2005 is acknowledged. Claims 1, 4-15 and 23-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 2-3 and 16-22 are under consideration in this office action.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim 17 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 17 does not further limit claim 16, since both claims are drawn to an immunogenic compositions.

Drawings

3. Figure 3 refers to sequences without sequence identifying numbers being described within the figure itself or the brief description of the drawings within the specification. Therefore, appropriate correction is requested.

Specification

4. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

5. The use of the trademarks TRIZOL™ and RNAsin™ have been noted in this application at page 19. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

6. Claims 3 and 16-22 are objected to because of the following informalities: The claims are dependent upon non-elected claims 1 and 4-11. Appropriate correction is required such that the claims are dependant upon only the elected claims.

7. Claims 16-22 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may refer in the alternative to only one set of claims. Claims such as claims 16 and 20 are improper. 35 U.S.C. 112 allows reference to only a particular claim. Furthermore, a multiple dependent claim may not serve as a basis for any other multiple dependent claims, either directly or indirectly. These limitations help to avoid undue confusion in determining how many prior claims are actually referred to in a multiple dependent claim. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 2-3 and 16-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a *Leishmania* protein involved in the virulence of the parasite, comprising at least one site (Cys-Gly-His-Cys) identical to the potential active

site of a protein from the protein disulfide-isomerase family (PDI) comprised within an immunogenic composition being capable of *in vitro* stimulation of the proliferation of mononuclear cells originating from individuals who have come into contact with a *Leishmania major* parasite or capable of inducing an immune response of the Th1 type when administered to a human or animal host. The protein is also comprised with a vaccinating composition wherein the composition is being intended to protect a human or animal host against leishmaniasis, and having a pharmaceutically acceptable formulation for administration to a human or animal host.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude, "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*,107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc. that set forth the claimed invention." *Lockwood,* 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.,* 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the

claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Furthermore, for broad generic claims, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.,* the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. *Fiers*, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In *Gostelli,* the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli,* 872 F.2d at 1012, 10 USPQ2d at 1618.

Claim 3 is drawn to a protein with any functional variant of LmPDI having at least 40% identity, preferably at least 80% identity with LmPDI. The written description in this case only sets forth specific sequences identified by their SEQ ID Numbers, therefore the written description is not commensurate in scope with the claims drawn to any

functional variant. Neither the specification nor the claims teach how to define any functional variant. Neither the claims nor the specification teach how to obtain such functional variants. There is no guidance as to what the functional variant are; or what functional variant can or cannot be used in the complex being claimed. The specification does not include structural examples. Thus, the resulting functional variant could result in complexes not taught and enabled by the specification. With the exception of specifically identified sequence, the skilled artisan cannot envision the detailed structure of the variants, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus.

Claims 2-3 drawn to the protein fails to recite any associated function. Without an associated function there is no limit on the protein encompassed by applicants claim. Furthermore any variant or mutant that has similar sequence identity yet has a different function is also encompassed by the claim. However, applicant has not taught examples of such proteins. Thus, the structure of sequences or functional variants have not defined but rather broaden the scope of the invention to encompass proteins not described by the instant specification.

Sequences having at least 40%, preferably at least 80% identity to SEQ ID NO:2, fail to meet the written description provision of 35 UCS 112, first paragraph. *Vas-Cath Inc. V. Mahurkar,* 19 USPQ2d 1111, make clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she

was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). The specification discloses SEQ ID NO: 2, there is no disclosure of sequences with at least 40, preferably at least 80% identity to SED ID NO: 2. Thus, the structure of these proteins or polypeptides is not defined. Even though the claims recite a sequence identification number, the skilled artisan cannot envision the detailed structure of the encompassed molecules since the specification has not defined what the 60% variability can be. Moreover, a skilled artisan cannot envision the detailed structure. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method for determining sequence identity. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of expression. The amino acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Currently the generic recitation of 40% identity, which lack a function of the protein is insufficient to support the claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Therefore, the full breadth of the claim fails to meets the written description provision of 35 USC 112, first paragraph.

With respect to claims 16-22 the claims are broad and require that the protein only have the four amino acids. It is well known in the art that one needs six to eight amino acids to make an epitope. With only four amino acids, no antibodies can bind to

the protein to thereby elicit an immune response. Applicants, have failed to describe an immunogenic or vaccinating composition comprising only those four amino acids which would be capable of *in vitro* stimulation of the proliferation of mononuclear cells originating from individuals who have come into contact with a *Leishmania major* parasite or capable of inducing an immune response of the Th1 type when administered to a human or animal host or that is intended to protect a human or animal host against leishmaniasis however, applicants have not described such compositions. The instant specification fails to provide any experiments that show that such compositions would be effective in protecting a human or other animal against a gram-negative bacterial infection. The term "vaccinating" encompasses the ability of the specific antigen to induce protective immunity to a bacterial infection or disease induction. The vaccine art is highly unpredictable and the instant specification fails to provide any information that the recited compositions would provide any immunity to patients against infection. There are still no immunological experiments provided to demonstrate that the claimed compositions are capable of mounting an effective immune response. More importantly, there are no challenge experiments to demonstrate that an animal immunized with the claimed compositions that would be protected from infection. It is well known that epitopes must be at least 6 to 8 amino acids in length in order to elicit an antibody response, however the instant protein has only four amino acids. There are no protocols detailing the amount of protein needed to mount a sufficient immune response. There is no teaching as to what the most effective route of administration for the claimed vaccines. There is merely a general outline of that does not apply directly to the instant invention. Therefore the specification fails to provide support for the claims. Moreover, it is noted that while immune responses may be generated in mice, it is also well known that merely generating an immune response does not equate to providing protective

immunity. This demonstration is required for the skilled artisan to be able to use the claimed compositions for their intended purpose of being capable of *in vitro* stimulation of the proliferation of mononuclear cells originating from individuals who have come into contact with a *Leishmania major* parasite or capable of inducing an immune response of the Th1 type when administered to a human or animal host or that is intended to protect a human or animal host against leishmaniasis. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed compositions, i.e. would not be able to accurately predict if protective immunity has been induced. The specification fails to teach the identity a compositions as claimed with the recited characteristics. Moreover, the specification lacks a sufficient variety of species to reflect this variance in the genus since the specification does not provide enough examples.

Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention. In view of these considerations, a person skilled in the art would not have viewed the teachings of the specification sufficient to show that applicants were in possession of a *Leishmania* protein involved in the virulence of the parasite, comprising at least one site (Cys-Gly-His-Cys) identical to the potential active site of a protein from the protein disulfide-isomerase family (PDI) comprised within an immunogenic composition being capable of *in vitro* stimulation of the proliferation of mononuclear cells originating from individuals who have come into contact with a *Leishmania major* parasite or capable of inducing an immune response of the Th1 type when administered to a human or animal host. The protein is also comprised with a vaccinating composition wherein the compositions is being intended to

protect a human or animal host against leishmaniasis, and having a pharmaceutically acceptable formulation for administration to a human or animal host. Therefore the full breadth of the claims fails to meet the written description provision of 35 USC 112, first paragraph.

9. Claims 2-3 and 16-22 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

The claims are drawn to a *Leishmania* protein involved in the virulence of the parasite, comprising at least one site (Cys-Gly-His-Cys) identical to the potential active site of a protein from the protein disulfide-isomerase family (PDI) comprised within an immunogenic composition being capable of *in vitro* stimulation of the proliferation of mononuclear cells originating from individuals who have come into contact with a *Leishmania major* parasite or capable of inducing an immune response of the Th1 type when administered to a human or animal host. The protein is also comprised with a vaccinating composition wherein the compositions is being intended to protect a human or animal host against leishmaniasis, and having a pharmaceutically acceptable formulation for administration to a human or animal host.

With respect to claim 3 which is drawn to a protein characterized in that it is the LmPDI protein of *Leishmania major*, with sequence SEQ ID NO:2 or any functional variant of LmPDI having at least 40% identity, preferably at least 80% identity with

LmPDI. However absent factual evidence, a percentage sequence similarity of less than 100% is not deemed to reasonably support, to one skilled in the art, as to whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. The art cited below teaches that replacement of a single amino acid residue may lead to both structural and functional changes in the biological activity of a protein. One of skill in the art would be reduced to merely randomly altering amino acids which would lead to unpredictable results regarding the functional activity of the polypeptide and the ability of the polypeptide to elicit an immune response. The art is replete with examples that even one amino acid change can lead to unpredictable changes in the biological activity of the protein. Therefore, the recitation of similar sequence identity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecules and the indicated similar biomolecule of known function and therefore lacks support regarding utility and/or enablement.

Several publications document the unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Russell [J. Mol. Bio.244:332-350]; Skolnick et al., [Trends in Biotech, 18(1):34-39]; and Attwood, [Science, 290:471-473, (29 October 2000)].

In absence of further guidance from Applicants, the skilled artisan would have to discover what the appropriate additions, deletion and substitutions would be. Such experimentation requires ingenuity beyond that expected of one of ordinary skill in the art. Such need for non-routine experimentation demonstrates that the specification is not enabled for any asserted use or well-established use of a sequence having at least 40% identity to LmPDI. The additions/deletions, substitutions or insertions of any amino acid in any location within the protein would not predictably result in an enabled polypeptide. The specification does not provide guidance on how any amino acids can be substituted or inserted for the production of a polypeptide nor does the specification provide guidance on how any location can be used to produce a stable polypeptide. No working examples are shown containing the missing information. Without such information, one of skill in the art could not predict which deletions, substitutions or insertions or any combination would result in the desired polypeptide. Accordingly, one of skill in the art would be required to perform undue experimentation to use any amino at any location to produce such proteins. Therefore, one skilled in the art could not make and/or use the invention without undue experimentation.

As to the asserted use of a *Leishmania* protein involved in the virulence of the parasite, comprising at least one site (Cys-Gly-His-Cys) identical to the potential active site of a protein from the protein disulfide-isomerase family (PDI) comprised within an immunogenic composition being capable of *in vitro* stimulation of the proliferation of mononuclear cells originating from individuals who have come into contact with a *Leishmania major* parasite or capable of inducing an immune response of the Th1 type

when administered to a human or animal host or the protein being comprised within a vaccinating composition wherein the composition is intended to protect a human or animal host against leishmaniasis, and having a pharmaceutically acceptable formulation for administration to a human or animal host, the specification lacks a clear demonstration that the protein of the instant claims is suitable for immunization. The specification states, at example 5 is drawn to using a recombinant LmPDI protein, however that passage does not provide support for administering a protein comprising only four amino acids and eliciting the claimed responses. Thus there is no evidence that the protein of the instant claims absent the same components will function at all to induce an immune response. There is no evidence that antibody production was elicited after administration of a polypeptide with at least 40% sequence identity to LmPDI. Therefore the effects of these changes are largely unpredictable and likewise present is the unreliable correspondence between the claimed protein and the recited administration of the LmPDI polypeptide, thus there is no support for the claims regarding enablement.

As previously, stated it is not clear that the alleged protein will elicit antibody production because epitopes must be at least 6 to 8 amino acids in length in order to elicit an antibody response, however the instant protein requires only four amino acids which is not enough to create an epitope. Absent clear demonstration of an immune response by a mammal as a result of receiving an immunogenetically effective amount of the protein, the protein could not be used in any well-established manner for inducing an immune response. In absence of further guidance from Applicants, the skilled artisan

would have to discover what the appropriate reagents are required, whether antibodies are even produced and whether this protein will function as an immunogen. Such experimentation requires ingenuity beyond that expected of one of ordinary skill in the art. Such need for non-routine experimentation demonstrates that the specification is not enabled for any asserted use or well-established use for isolated polypeptides. Accordingly, the specification is not enabled for using the alleged protein in any manner disclosed. Therefore, a skilled artisan would be forced into undue experimentation to practice (i.e., make and use) the invention as is broadly claimed.

10. Claims 2-3, and 16-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 2 recites the limitations "the potential active site " and "the protein disulfide isomerase" in the claim. The suggested claim language is to use of the article "a" such that the language is "a potential active site " and "a protein disulfide isomerase." There is insufficient antecedent basis for this limitation in the claim.

b) Claim 3 recites the limitation "the LmPDI protein of Leishmania major " in the claim. The suggested claim language is to use of the article "a" such that the language is "a LmPDI protein of Leishmania major. " There is insufficient antecedent basis for this limitation in the claim.

c) In claim 3, acronyms like LmPDI must be spelled out when used for the first time in a chain of claims.

d) In claim 3, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 3 recites the broad recitation having at least 40%, and the claim also recites at least 80% which is the narrower statement of the range/limitation.

e) Dependant claims 3, 17-19 and 21-22 refer to "a protein" or "an immunogenic l composition" or " a vaccinating composition" however the suggested claim language is to use of the article "the." Therefore the suggested claim language is "the protein" or "the immunogenic composition" or "the vaccinating composition."

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 2-3 are rejected under 35 U.S.C. 101 because a *Leishmania* protein which comprises at least one site (Cys-Gly-His-Cys) as described by the claim is a product of nature and is naturally produced. The claims do not require that the *Leishmania* protein to be isolated. Insertion of the terms "isolated or purified" would obviate this rejection.

Prior Art

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Achour et al., teach the identification of a disulfide isomerase protein of *Leishmania major* as a putative virulence factor. Ivens et al., teach a physical map of the *Leishmania major* friedlin genome. Ravel et al., teach the complete chromosomal organization of the reference strain of the *Leishmania* Genome Project, *L. major* 'Friedlin.' Stiles et al., teach genomic organization, transcription, splicing and gene regulation in *Leishmania*.

Conclusion

13. No claims allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines

October 25, 2005